

**REMARKS UNDER 37 CFR § 1.111**

**Formal Matters**

Claims 1-4 and 6-15 are pending after entry of the amendments set forth herein.

Claims 1-7 were examined. Claims 1-7 were rejected.

Claims 1, 2 and 4 are amended. The amendments to the claims were made solely in the interest of expediting prosecution, and are not to be construed as an acquiescence to any objection or rejection of any claim. Support for the amendments to the claims is found in the claims as originally filed, and throughout the specification, in particular at the following exemplary locations: line 30 on page 4. Accordingly, no new matter is added by these amendments.

Please replace claims with the claim set provided above.

Claims 5 is canceled without prejudice to renewal, without intent to acquiesce to any rejection, and without intent to surrender any subject matter encompassed by the canceled claims. Applicants expressly reserve the right to pursue any canceled subject matter in one or more continuation and/or divisional applications.

Applicants respectfully request reconsideration of the application in view of the remarks made herein.

**PTO 1449 form**

Applicants respectfully request that the Examiner initial and return the PTO 1449 form submitted with the Information Disclosure Statement filed herewith, thereby indicating that the references cited therein have been reviewed and made of record.

**Claim Objections**

Claim 5 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of the previous claim.

The Applicants disagree with the rejection. However, solely to expedite prosecution, the Applicants have cancelled claim 5, and, as such, this rejection is now moot.

**Rejection under 35 U.S.C. §101 and §112, ¶1**

Claims 1-8 are rejected under 35 USC §101, assertedly because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility. Claims 8 are further rejected under 35 USC 112, first paragraph assertedly because one of skill in the art would not know how to use the claimed invention if its lacks utility. Since both rejections are established using the same reasons, Applicants respectfully traverse these rejections together.

The rejection appears to be based on the assertion that there are no data relating to the function of the claimed polynucleotides in the instant patent application.

The Applicants respectfully submit that Table 5 of the instant application represents data that shows that the claimed polynucleotides are differentially expressed in colon cancer. For the Examiner's convenience, a copy of the relevant pages of Table 5 with highlighted data relating to SEQ ID NO:222 is attached herewith. According to the data, a gene corresponding to a claimed polynucleotide is expressed at approximately 10-fold greater amounts in metastasized colon cancer cells as compared to normal colon cells, and expressed at approximately 20-fold greater amounts in metastasized colon cells as compared to non-metastasized colon cells. As such, and to summarize in a simplified manner, the claimed polynucleotides represent a gene that is differentially expressed in cancerous cells. Genes that are differentially expressed in cancerous cells have utility as, for example, a diagnostic for detecting a cancerous cell.

The Applicants respectfully submit that this data therefore establishes a credible, specific and substantial utility for the claimed invention.

In view of the credible, specific and substantial utility of the claimed polynucleotides, Applicants respectfully request that the rejection of claims 1-8 under 35 U.S.C. § 101 and 35 U.S.C. § 112, first paragraph, be withdrawn.

**Rejection under 35 U.S.C. §112, first paragraph (written description)**

Claims 1-8 are rejected under 35 U.S.C. §112, first paragraph as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In making the rejection, the Office cited *Amgen, Inc. v. Chugai Pharmaceutical Co.*, *Fiers v. Revel*, *Fiddes v. Baird*, and *University of California v. Eli*

*Lilly and Co.* This rejection is traversed as applied and as it may apply to the presently pending claims.

The presently pending claims are directed to polynucleotides, recombinant host cells, vectors, polynucleotide sequences of inserts contained in ATCC deposited clones, methods of making polypeptides, and cDNAs produced by amplification using a fragment of a specific sequence. The polynucleotide sequences that are the basis for these claims are differentially expressed in cancerous cells relative to normal, non-cancerous cells.

*The Office has Not Met Its Burden of Establishing a Prima Facie Case of Lack of Written Description*

The inquiry for adequacy of written description is whether one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention at the time the application was filed. The courts have held that there is a “strong presumption” that an adequate written description of the claimed invention is present when the application is filed.<sup>1</sup> The Office “has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims.”<sup>2</sup> With respect to this burden, the Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, ¶1, “Written Description” Requirement, state:

A description as filed is **presumed to be adequate, unless or until sufficient evidence or reasoning to the contrary has been presented by the examiner to rebut the presumption.** The examiner, therefore, must have a **reasonable basis** to challenge the adequacy of the written description. The examiner has the **initial burden** of presenting by a **preponderance of evidence** why a person skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims. In rejecting a claim, the examiner must set forth **express findings of fact** regarding the above analysis which support the lack of written description conclusion. These findings should:

- (1) Identify the claim limitation at issue; and
- (2) **Establish a prima facie case by providing reasons** why a person skilled in the art at the time the application was filed would not have recognized that the inventor was in possession of the invention as claimed in view of the disclosure of the application as filed. **A general allegation of "unpredictability in the art" is not a sufficient reason**

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<sup>1</sup> See, e.g., *In re Wertheim*, 541 F.2d 257 (CCPA 1976).

<sup>2</sup> *Id.* at 263.

**to support a rejection for lack of adequate written description.**<sup>3</sup>  
(emphasis added)

Applicants respectfully submit that the Office's burden has not been met and that the specification provides adequate written description of the claimed invention such that one of skill in the art would recognize that Applicants' had possession of the claimed invention.

The Office has not provided "**sufficient evidence or reasoning to the contrary...to rebut the presumption**" of adequacy of the written description.<sup>4</sup> In fact, the Office has presented no evidence whatsoever as to why a person of skill in the art would not recognize Applicants' possession of the claimed invention. None of those cases establish why the skilled artisan would not recognize Applicants' possession. The Office provided no other evidence.

In sum, the Office has failed to establish a *prima facie* case of lack of written description. Applicants' specification presumptively provides an adequate written description and the Office has failed to present adequate grounds to sustain a written description rejection, providing little more than conclusory statements and vague assertions. Applicants' thus submit that the presently pending claims meet the written description requirement and that this rejection of the claims under 35 U.S.C. §112, first paragraph, should be withdrawn. This simple point overcome the rejections. To the extent a further discussion is believed necessary, the Examiner is respectfully referred to the following.

The Office attempts to rely on the following four Federal Circuit and Board of Patent Appeals and Interferences cases in support of its assertion that the invention lacks written description.

*Amgen, Inc. v. Chugai Pharmaceutical, Co.*

In *Amgen, Inc. v. Chugai Pharmaceutical, Co.*, Amgen sued Genetics Institute and Chugai Pharmaceuticals for patent infringement. The Amgen patent issued on October 27, 1987 and contained claims to the DNA sequence encoding human erythropoietin (EPO). Amgen claimed priority of invention based on isolation of EPO clones in 1983.<sup>5</sup>

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<sup>3</sup> 66 Fed. Reg. 1107 (January 2001).

<sup>4</sup> *Id.*

<sup>5</sup> 927 F.2d 1200 (Fed. Cir. 1991).

Prior to Amgen's cloning of the EPO gene, however, Genetics Institute had isolated and purified the EPO protein and had also disclosed a possible method of purifying and isolating the EPO DNA sequence.<sup>6</sup> The USPTO issued a patent to Genetics Institute on June 30, 1987 containing claims to the EPO protein itself.<sup>7</sup> Genetics Institute did not actually clone the EPO cDNA until August 1984, and began making recombinant EPO using the cDNA shortly thereafter.<sup>8</sup>

The Federal Circuit held that the Amgen patent was not invalidated based on the earlier disclosure by Genetics Institute of a probing strategy to screen a DNA library for the EPO coding sequence, even though this strategy eventually resulted in the actual cloning of the gene by Genetics Institute.<sup>9</sup> Genetics Institute's disclosure of the protein, and a method for isolating and purifying the EPO DNA sequence, was insufficient to constitute actual conception of the DNA encoding EPO.<sup>10</sup> Applying chemical case law precedent,<sup>11</sup> the Amgen court stated:

A gene is a chemical compound, albeit a complex one, and it is well established in our law that conception of a chemical compound requires that the inventor be able to **define it so as to distinguish it from other materials**, and to describe how to obtain it. Conception does not occur unless one has a mental picture of the **structure of the chemical**, or is able to **define it by its method of preparation**, its physical or chemical properties, or **whatever characteristics sufficiently distinguish it**. It is not sufficient to define it solely by its principle biological property, *e.g.*, encoding human erythropoietin, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property.<sup>12</sup> (emphasis added)

Thus, since Genetics Institute had not yet cloned the DNA sequence encoding EPO when it filed its patent application, and the specification only suggested a possible method by which to isolate the DNA sequence, Genetics Institute could not have a mental conception of the EPO DNA sequence at the time the application was filed.<sup>13</sup> The court did not invoke the requirement that

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<sup>6</sup> *Id.* at 1205.

<sup>7</sup> *Id.* at 1203.

<sup>8</sup> *Id.* at 1205-06.

<sup>9</sup> *Id.* at 1206.

<sup>10</sup> *Id.*

<sup>11</sup> See *Oka v. Youssefieh*, 849 F.2d 581, 583 (Fed. Cir. 1988). The court, in *Amgen*, classified DNA as a complex chemical compound and held that "it is well established in our law that conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials, and ... describe how to obtain it." *Amgen*, 927 F.2d at 1206.

<sup>12</sup> *Amgen*, 927 F.2d at 1206 (citations omitted).

<sup>13</sup> *Id.*

the actual DNA sequence be disclosed, but only that the DNA be defined in a way to distinguish it from other chemicals along with a description of how to obtain it.<sup>14</sup>

*Fiers v. Revel*

In 1993, the Federal Circuit applied the holding in *Amgen* to an interference case where three parties (Fiers, Revel, and Sugano) claimed patent rights to the DNA encoding human fibroblast beta interferon (IFN- $\beta$ ). In *Fiers v. Revel*,<sup>15</sup> Fiers asserted priority based on his conception of a method for isolating the IFN- $\beta$  DNA in 1979 or early 1980, coupled with due diligence towards a constructive reduction to practice on April 3, 1980.<sup>16</sup> Before he isolated the DNA, Fiers had disclosed his method to two American scientists, both of whom submitted affidavits that Fiers' method would have allowed a person of ordinary skill in the art to isolate the IFN- $\beta$  DNA sequence without undue experimentation.<sup>17</sup>

Fiers asserted that the stringent written description requirement set forth in *Amgen* only applied when the disclosed method for isolating a DNA sequence could not easily be carried out by one of ordinary skill in the art.<sup>18</sup> Fiers also argued that *Amgen* allows conception of a DNA sequence by its method of isolation.<sup>19</sup> The Federal Circuit rejected both of these arguments, stating that Fiers was focusing inappropriately on the issue of enablement rather than written description.<sup>20</sup> The court also stated that, before reduction to practice, conception only of a process for making a substance, without a **conception of a structural or equivalent definition** of that substance, cannot constitute more than conception of the substance claimed as a process (product-by-process claim).<sup>21</sup> **Conception of a substance claimed *per se*, without reference to a process requires conception of its structure, name, formula, or definitive chemical or physical properties.**<sup>22</sup>

Revel sought to use the benefit of a 1979 Israeli application as a constructive reduction to practice to prove priority of invention for IFN- $\beta$  DNA. The court held that the Israeli application

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<sup>14</sup> *Id.*

<sup>15</sup> 984 F.2d 1164, 1166 (Fed. Cir. 1993).

<sup>16</sup> *Id.*

<sup>17</sup> *Id.*

<sup>18</sup> *Id.* at 1169.

<sup>19</sup> *Id.*

<sup>20</sup> *Id.*

<sup>21</sup> *Id.*

did not contain an adequate written description of a DNA encoding IFN- $\beta$  because it only disclosed a method for isolating a fragment of the DNA coding for IFN- $\beta$  and a method for isolating IFN- $\beta$  mRNA.<sup>23</sup> The court concluded:

An adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself....Revel's application does not even demonstrate that the disclosed method actually leads to the DNA, and thus that he had possession of the invention, since it only discloses a clone that might be used to obtain mRNA coding for [IFN- $\beta$ ]. A bare reference to a DNA with a statement that it can be obtained by reverse transcription is not a description; it does not indicate that Revel was in possession of the DNA.<sup>24</sup>

The court went on to note that the reasoning applied in *Amgen*, with respect to what is necessary to show conception, also applies to the adequacy of descriptions of DNA:

As we stated in *Amgen* ... such a disclosure just represents a wish, or arguably a plan, for obtaining the DNA. If a conception of a DNA requires a **precise definition, such as by structure, formula**, chemical name, or physical properties, ... then a description also requires that degree of specificity.... [O]ne cannot describe what one has not conceived.<sup>25</sup>

Thus, it appears from the *Fiers* decision that there must be some specific characterization of the DNA itself to convey to one skilled in the art that the inventor was in possession of the DNA at the time of filing. The court ultimately held that Sugano, another party in the action, was entitled to priority because the disclosure in his 1980 application contained the DNA which codes for IFN- $\beta$ , along with a detailed disclosure of the method used to obtain that DNA.<sup>26</sup>

#### *Fiddes v. Baird*

The Office also relies on the 1993 decision in *Fiddes v. Baird*,<sup>27</sup> in which the Board of Patent Appeals and Interferences cited *Fiers* in a priority contest over inventorship of recombinant DNA molecules encoding fibroblast growth factors ("FGFs"). Baird claimed priority on the basis of an application that set forth the amino acid sequence for bovine pituitary FGF and a *theoretical* DNA sequence encoding that protein, along with a method for obtaining a

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<sup>22</sup> *Id.*

<sup>23</sup> *Id.* at 1167.

<sup>24</sup> *Id.* at 1170-71.

<sup>25</sup> *Id.* at 1171.

<sup>26</sup> *Id.*

<sup>27</sup> 30 USPQ2d 1398 (BPAI 1993).

cDNA corresponding to the protein. The application did not teach the actual naturally-occurring DNA sequence encoding the FGF protein.<sup>28</sup> Since the nucleotide sequence of the naturally-occurring DNA molecule was not sufficiently disclosed, the Board followed *Fiers* in determining that Baird was not in possession of the broad class of naturally-occurring genes encoding mammalian FGFs:

An adequate description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; **what is required is a description of the DNA itself.**

\* \* \*

If a conception of a DNA requires a **specific definition, such as by structure, formula**, chemical name, or physical properties, as we have held, then a description also requires that degree of specificity....[O]ne cannot describe what one has not conceived.<sup>29</sup> (emphasis added)

The Board further stated that “knowledge of the amino acid sequence of a protein coupled with the established relationship in the genetic code between a nucleic acid and the protein it encodes would not establish possession of the gene encoding that protein.”<sup>30</sup>

*Regents of the University of California v. Eli Lilly & Co.*

The most recent case cited by the Office to support its assertion that the invention fails to meet the written description requirement is *Regents of the University of California v. Eli Lilly & Co.*<sup>31</sup> In 1977, the University of California (UC) cloned the rat insulin gene and filed a patent application that same year claiming the rat and human insulin genes, as well as broadly claiming all mammalian and vertebrate insulin genes.<sup>32</sup> After a patent issued to UC on the insulin gene in March 24, 1987 (U.S. Patent No. 4,652,525), UC filed suit against Eli Lilly for patent infringement for its sale of synthetic human insulin.<sup>33</sup> Claims 2, 4, and 5 of the ‘525 patent were as follows:

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<sup>28</sup> *Id.* at 1482-81.

<sup>29</sup> *Id.* at 1482-83, citing *Fiers*, 984 F.2d at 1170-71.

<sup>30</sup> *Id.*

<sup>31</sup> 119 F.3d 1559 (Fed. Cir. 1997).

<sup>32</sup> *Id.* at 1562-63.

<sup>33</sup> *Id.* at 1562.

2. A recombinant procaryotic microorganism modified to contain a nucleotide sequence having the structure of the reverse transcript of an mRNA of a vertebrate, which mRNA encodes insulin.
4. A microorganism according to claim 2 wherein the vertebrate is a mammal.
5. A microorganism according to claim 2 wherein the vertebrate is a human.

UC thus claimed all vertebrate, mammalian, and human insulin cDNA sequences.

The Federal Circuit, relying on its reasoning in *Fiers*, held that the broad claims of the '525 patent were invalid for lack of a written description.<sup>34</sup> The court reasoned that a description of rat insulin cDNA is not a description of vertebrate, mammalian, or human cDNA.<sup>35</sup> Likewise, the court reasoned that the mere name "mammalian insulin cDNA" in a claim is not an adequate description because it describes the function of the gene, but not its structure.<sup>36</sup> The court went on:

In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. **One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass.** Accordingly, **such a formula is normally an adequate description** of the claimed genus. In claims to genetic material, however, a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus....

Thus, as we have previously held, a cDNA is not defined or described by the mere name "cDNA," even if accompanied by the name of the protein that it encodes, but requires a kind of specificity usually achieved by means of the recitation of the sequence of nucleotides that make up the cDNA. A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or **of a recitation of structural features common to the members of the genus**, which features constitute a substantial portion of the genus... We will not speculate in what other ways a broad genus of genetic material may be properly described, but it is clear to us... that the genera of vertebrate and mammal cDNA are not described by the general language of the '525 patent's written description

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<sup>34</sup> *Id.* at 1566-69.

<sup>35</sup> *Id.* at 1568.

<sup>36</sup> *Id.* at 1568.

supported only by the specific nucleotide sequence of rat insulin.<sup>37</sup> (emphasis added)

Thus, while the '525 patent specification contained adequate written description of the rat insulin cDNA, this description did not give UC a right to also claim the cDNA encoding all vertebrate or mammalian insulin. Describing one member of the genus, without reciting structural features common to the members of the genus, does not give the inventor a right to claim the entire genus, only that one member. The '525 patent provided no sequence information for the claimed human insulin cDNA. Simply providing a general method of producing human insulin cDNA and a description of the human insulin amino acid sequence that cDNA encodes, does not provide a written description of human insulin cDNA.<sup>38</sup>

*The Facts of the Cited Cases are Distinct from those of the Instant Application*

None of the four cases discussed above provide a situation analogous to the one at hand. In all four cases, a party was attempting to broadly claim a DNA sequence based on the amino acid sequence of the encoded protein or on the DNA sequence encoding the protein from a different animal. In no case had the party provided a sequence that was present in all members of the claimed genus of sequences or a structural characteristic common to all members of the claimed genus. As such, the party could not describe the sequence "so as to distinguish it from other materials" as required by the courts. None of the four cases are analogous to the instant application.

As stated in *Amgen*, DNA is simply a chemical compound that can be conceived of by a mental picture of the structure of the compound or whatever characteristics sufficiently distinguish it. In *Lilly*, the court stated that in claims involving chemical materials, generic formulae must indicate with specificity what the claims encompass such that one skilled in the art can **distinguish the formula from other formulas and can identify many of the species the claims encompass**. Such a formula generally constitutes an adequate written description of the claimed genus. *Lilly* also held that a **description of a genus of cDNAs may be achieved by recitation of structural features common to the members of the genus**. Moreover, the court

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<sup>37</sup> *Id.* at 1568-69.

<sup>38</sup> *Id.* at 1567.

in *Fiers* held that conception of a substance requires conception of its structure, formula, or definitive chemical or physical properties.

*The Applicants of the Instant Application have Provided Nucleotide Sequences that Define the Claimed Polynucleotides*

In the instant application, Applicants have provided specific nucleotide sequences that represent a distinguishing structural feature common to the genus of claimed polynucleotides. The provided sequences are the structural features that are common to the members of the claimed genus and serve to define the claimed genus. For example, claim 1 is directed to an isolated polynucleotide comprising at least 50 contiguous nucleotides of SEQ ID NO:222, or complement thereof which hybridizes under stringent conditions to a polynucleotide having the sequence of SEQ ID NO:222 or complement thereof. With the knowledge of the nucleotide sequence of SEQ ID NO: 222, one skilled in the art can easily determine if a sequence is a member of the claimed genus.

This sequence recited in the claims provides the claimed invention with a critical defining feature – one that was said to be lacking in the claims considered and rejected in each of *Amgen*, *Fiers*, *Lilly*, and *Fiddes*. The sequence recited in the claims defines the claimed polynucleotide “so as to distinguish it from other materials.”<sup>39</sup> The recited sequence also provides “a structural or equivalent definition” of the claimed polynucleotide.<sup>40</sup> Moreover, the sequence recited in the claims provides “a recitation of structural features common to the members of the [claimed] genus.”<sup>41</sup> Thus, it is much more than a mere wish to obtain a composition – it defines the composition.

The polynucleotides of the invention are also claimed in product-by-process claims, which are directed to an isolated cDNA obtained by the process of amplification using a polynucleotide comprising at least a specific number of nucleotides of a nucleotide sequence of a specific SEQ ID NO. Product-by-process claims are a well-accepted alternative way for applicants to claim their inventions.<sup>42</sup> These claims are in keeping with the law as expressed by

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<sup>39</sup> *Amgen*, 927 F.2d at 1206.

<sup>40</sup> *Fiers*, 984 F.2d at 1169. See also *Fiddes*, 30 USPQ2d at 1482-83.

<sup>41</sup> *Lilly*, 119 F.3d at 1568-69.

<sup>42</sup> See, e.g., *In re Hughes*, 496 F.2d 1216 (CCPA 1974); *In re Bridgeford*, 357 F.2d 697 (CCPA 1966); Chisum §8.05.

the court in *Amgen*, which stated that a DNA sequence can be defined by its method of preparation.

With regard to product-by-process claims, the Office asserts that “merely claiming a composition in a product by process format does not relieve the applicants from the duty of providing adequate written description of the claimed product.” As explained above, however, the Applicants have provided a sequence, which sequence serves to define the claimed invention. Thus, one skilled in the art can envision the sequences that would be obtained by a process of amplification using a polynucleotide for which the sequence has been provided.

The application also contains claims to inserts of ATCC-deposited clones. These clone inserts are fully described in the application, and they comprise a sequence of a SEQ ID NO described in the application. Accordingly, one of skill in the art would reasonably conclude that Applicants had possession of the claimed invention at the time the application was filed.

### *Conclusion*

The claims of the instant application are supported by an adequate written description. The Office has provided no evidence to establish that one of skill in the art would not recognize that Applicants had possession of the claimed invention at the time the application was filed. The four cases cited in support of the Office’s assertions in the original rejection did not address a situation similar to the one at hand, where common structural features have been provided for all members of the claimed genera.

As stated above, the claimed genera of polynucleotides are defined by common structural characteristics such that one skilled in the art can easily determine whether a sequence falls within a claimed genera, can envision a multitude of sequences having that structural characteristic common to a claimed genera, and would thus recognize that Applicants had possession of the claimed genera at the time of filing. Moreover, as noted above, the Office has failed to provide the “sufficient evidence or reasoning” necessary to support a written description rejection. Conclusory statements can not, standing alone, constitute a *prima facie* case of lack of written description. Accordingly, Applicants respectfully request withdrawal of this rejection of the claims under 35 U.S.C. §112, first paragraph.

**Rejection under 35 U.S.C. §112, first paragraph (enablement)**

Claim 3 is rejected under 35 U.S.C. §112, first paragraph as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, the Office Action asserts that the deposits are not in full compliance with 37 C.F.R. §§ 1.803-1.809.

A Statement of Availability is enclosed stating that the clones shown in Tables 7 and 8 of the instant application are deposited and publicly available. As such, since the clone referenced in Claim 3 is listed in Tables 7 and 8 of the instant application, it is deposited and publicly available.

Applicants submit that the rejection of Claim 3 under 35 USC 112, first paragraph have been addressed by this foregoing remarks, and the rejection may be withdrawn.

**Rejection under 35 U.S.C. §102**

Claims 1, 2 and 4-7 are rejected under 35 U.S.C. §102(b) as being anticipated by database record AI459918 (deposited 3/1/1999). Specifically, the Office Action asserts that AI459918 comprises 49 contiguous nucleotides of SEQ ID NO:222 and would hybridize to it, therefore anticipating the claims. This rejection is traversed as applied and as it may apply to the presently pending claims.

Claim 1, 2 and 4 are amended to recite a polynucleotide that comprises 50 contiguous nucleotides of SEQ ID NO:222 or complement thereof.

Since AI459918 comprises only 49 contiguous nucleotides of SEQ ID NO:222 or complement thereof, and not 50 contiguous nucleotides of SEQ ID NO:222 or complement thereof as the claims require, AI459918 cannot anticipate the claims.

The Applicants respect that this rejection has been adequately addressed. Accordingly, this rejection of claims 1, 2 and 4-7 under 35 U.S.C. § 102 may be withdrawn.

Claims 1, 2 and 4-7 are rejected under 35 U.S.C. §102(b) as being anticipated by database record AA743908 (deposited 2/19/1998). Specifically, the Office Action asserts that AA743908 comprises 49 contiguous nucleotides of SEQ ID NO:222 and would hybridize to it,

therefore anticipating the claims. This rejection is traversed as applied and as it may apply to the presently pending claims.

Claim 1, 2 and 4 are amended to recite a polynucleotide that comprises 50 contiguous nucleotides of SEQ ID NO:222 or complement thereof.

Since AA743908 comprises only 49 contiguous nucleotides of SEQ ID NO:222 or complement thereof, and not 50 contiguous nucleotides of SEQ ID NO:222 or complement thereof as the claims require, AI459918 cannot anticipate the claims.

The Applicants respect that this rejection has been adequately addressed. Accordingly, this rejection of claims 1, 2 and 4-7 under 35 U.S.C. § 102 may be withdrawn.

**CONCLUSION**

Applicant submits that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number 2300-1624.

Respectfully submitted,  
BOZICEVIC, FIELD & FRANCIS LLP

Date: May 2, 2003

By: James S. Keddie  
James S. Keddie, Ph.D.  
Registration No. 48,920

BOZICEVIC, FIELD & FRANCIS LLP  
200 Middlefield Road, Suite 200  
Menlo Park, CA 94025  
Telephone: (650) 327-3400  
Facsimile: (650) 327-3231

Table 5

SEQ	CLST	Library Pair A,B	A	B	A/B	B/A
		15,17 (Normal Colon Tissue vs. Colon Metastasis)	8	0	8.59	
		16,17 (Colon Tumor Tissue vs. Colon Metastasis)	7	0	7.11	
213	557401					
		15,17 (Normal Colon Tissue vs. Colon Metastasis)	10	2	5.37	
214	455155					
		15,16 (Normal Colon vs. Colon Tumor Tissue)	12	3	4.23	
215	551117					
		16,17 (Colon Tumor Tissue vs. Colon Metastasis)	0	6		5.91
217	729295					
		15,16 (Normal Colon vs. Colon Tumor Tissue)	0	7		6.62
		16,17 (Colon Tumor Tissue vs. Colon Metastasis)	7	0	7.11	
218	450429					
		16,17 (Colon Tumor Tissue vs. Colon Metastasis)	10	1	10.16	
		15,17 (Normal Colon Tissue vs. Colon Metastasis)	13	1	13.95	
219	450148					
		16,17 (Colon Tumor Tissue vs. Colon Metastasis)	0	6		5.91
220	380412					
		15,17 (Normal Colon Tissue vs. Colon Metastasis)	6	0	6.44	
		15,16 (Normal Colon vs. Colon Tumor Tissue)	6	0	6.34	
221	446614					
		16,17 (Colon Tumor Tissue vs. Colon Metastasis)	7	0	7.11	
222	555911					
		15,17 (Normal Colon Tissue vs. Colon Metastasis)	2	21		9.78

Table 5

SEQ	CLST	Library Pair A,B	A	B	A/B	B/A
		16,17 (Colon Tumor Tissue vs. Colon Metastasis)	1	21		20.68
223	450828					
		15,17 (Normal Colon Tissue vs. Colon Metastasis)	1	9		8.38
224	28					
		18,20 (Normal Colon Tissue vs. Colon Metastasis)	2	11		6.43
		18,19 (Normal Colon Tissue vs. Colon Tumor)	2	43		18.81
		15,17 (Normal Colon Tissue vs. Colon Metastasis)	53	207		3.64
		03,04 (Breast, High Met vs. Breast, Non-Met)	697	1789		2.63
		19,20 (Colon Tumor Tissue vs. Colon Metastasis)	43	11	2.92	
225	446450					
		15,16 (Normal Colon vs. Colon Tumor Tissue)	11	3	3.88	
226	452026					
		15,16 (Normal Colon vs. Colon Tumor Tissue)	35	14	2.64	
227	643594					
		15,16 (Normal Colon vs. Colon Tumor Tissue)	7	0	7.4	
		15,17 (Normal Colon Tissue vs. Colon Metastasis)	7	0	7.51	
228	1905					
		01,02 (Colon, High Met vs. Colon, Low Met)	7	21		3.25
		15,17 (Normal Colon Tissue vs. Colon Metastasis)	0	7		6.52
229	651073					
		15,17 (Normal Colon Tissue vs. Colon Metastasis)	7	0	7.51	
		15,16 (Normal Colon vs. Colon Tumor Tissue)	7	0	7.4	
230	553705					
		15,16 (Normal Colon vs. Colon Tumor Tissue)	12	0	12.68	